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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/741,814	12/22/2000	Rene C. Gaudreault	PA-153	9015

7590 06/17/2003

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EXAMINER
VOLLANO, JEAN F

ART UNIT	PAPER NUMBER
1621	

DATE MAILED: 06/17/2003

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/741,814	GAUDREAULT ET AL.	
	Examiner	Art Unit	
	Jean F. Vollano	1621	

-- Th MAILING DATE of this communication appears on the cover sh t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-8* is/are pending in the application.

4a) Of the above claim(s) *1-3 and 5-7* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The amendment filed 4/30/2003, has been entered. Claim 4 has been canceled and non elected claims 1-3,5-7 and newly added claim 8 are pending. As stated before claim 1-3 and 5-7 are withdrawn from consideration as being drawn to non elected subject matter. It would hasten prosecution if the non elected subject matter were canceled.

2. Since the original claim 4 which was examined has been canceled and replaced by another claim 8 which is also a method claim the examiner will withdrawn all the previous rejections and rewrite those that are applicable to the new claim as written such as the 112, 2 rejection over the term "prodrugs thereof." The examiner notes applicant has made no response to this rejection and has place the same language in the new claim.

Claim Rejections - 35 U.S.C. § 112

3. Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 8 recites the limitation of " targeting protein receptors as found in a human carcinoma cell line," The examiner cannot find this language anywhere in the specification and applicant has not given support for the language based on the specification. There is a human breast cancer carcinoma mentioned. But this is not all carcinomas nor is it clear that the breast cancer carcinoma was used as an assay for targeting protein receptors. It appears that the testing was for protein alkylation. Please either show support for a method targeting protein receptors as found in a human carcinoma cell line or eliminate the new matter. This problem also occurs in section ii) of the claim. Also should the claim be directed to "selectively targeting" which was the language in the original claim and in the specification as amended.

Also in the original claim and the newly added portion of the specification has "ii) testing said molecules against various cell receptors." Now the claim has "incubating the human carcinoma cell line with the compound of formula I, to provide incubated cells." It is unclear where support for this change in the methodology comes from in the specification. The filing of the specification and claims must contain the invention as it is being claimed to show that applicant had possession of the claimed invention at the time of filing. This language or support for this language must be in the specification as filed. The examiner does not find this support in the specification and applicant has not shown where there is support for this limitation. The same problem occurs with the detecting step iii). The whole language is quite different from the original claim. Please show support or remove the new matter.

The examiner notes that the claim language seems more of an evaluation of cytotoxic activity than a targeting scheme. Targeting usually involves preparing a compound or composition to go to a specific tumor or tumor site. The examiner also notes this seem very similar to alkylation at the protein receptor site.

4. Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 recites the limitation of "molecule of formula I, prodrugs thereof". A prodrug is usually a protected group which cleaves after the drug is in the body. For example and ester can be a prodrug of an acid which hydrolyzes to the acid in the body or cell culture. However in this instance there is a formula which has alkyl groups, a halogen on a carbon chain and two nitrogens as part of a urea moiety, and it is unclear what is meant as the metes and bounds of the term " prodrug" in this instance. The specification gives little guidance and talks about sulfoxide or sulfone derivatives as prodrugs but does not specify even where the sulfoxide or sulfone derivative would be on the molecule. Would it be on the ring or would it be as a counter ion of an acidic nitrogen environment? Could the prodrug include a aziridine type ring that could be opened up and then halogenated to form the ethylene chloro compound ? Could a prodrug be a transition metal complex which releases the metal upon dissolution in the body? The term prodrug is confusing as written (in view of the chemical compound and the specification) as to the metes and bounds of what is being claimed.

Claim 8 recites "the protein". This lacks antecedent basis since no protein had previously been mentioned.

Claim 8 recites the limitation of "measuring inactivation of the protein". This is a methodology which should be clear and concise. The measuring of the inactivation of the protein is a major step. However it is unclear how one measures this inactivation. Is it by any method commonly known in the art? Is it by colorimetric techniques? Is it by NMR techniques, or flow cytometry, gel migration studies? There seems also to be an omission of an essential step even if the step is just performed by methods commonly known in the art. Please give support for any modification of the claim.

5. In reference to the new cell line being claim in the methodology which is a cancer cell line the examiner will review the literature in terms of the newly added claim for carcinoma cell lines as written with the potential new matter in it.

US 5,530,026 and 5,750,547 cited on the PTO 1449 teach some compounds of instant claim 1 as cancer agents and shows ID_{50} for the compounds in human adenocarcinoma cells, ovarian carcinoma cells and human breast cancer cells. There is no method described for method for selectively targeting a particular protein site and measuring the inactivation of the protein.

Anticancer research -1988 cited on the PTO 1449 form teaches activity in vitro and in vivo of antineoplastic agents which are 1-aryl 3-(2-chloroethyl) ureas. The reference uses a

mutagenicity assay, toxicity assay, and antineoplastic assay to determine the efficacy of the compounds.

Cancer Chemother Parmacol- 1994 cited on the PTO 1449 teaches compounds of formula I in the instant invention used as a study with human breast carcinoma cell line MCF-7-ADRr. The MCF-7ADRr has a major mechanism associated with resistance of P-glycoprotein-mediated decrease in drug accumulation.

Anticancer Research 1993 cited on the PTO 1449 teaches metabolic studies on proteins Tubulin and Vimentin by a compound of formula 1 which is 4-ter-butyl[3-(-2-chloroethyl)ureido] benzene (tBCEU). The chemical structure of (TBCEU) is characterised by the presence of an alkyl substituted position which is analogous to the moiety of nitrogen mustard. tBCEU induces protein synthesis in response to treatment of the human breast cancer cell line MBA-MB-231). However by altering the stability of tubulin mRNA it was observed that tBCEU decreases the tubulin and the feedback response to the deceasing amount of free tublin may trigger cells to synthesize more of the tubulins ultimately leading to autoregulation. The process seems in part the same to the extent of making the compound incubating the human carcinoma cells with the compound to provide incubated cells but there is no detection of binding of the protein receptors by measuring the inactivation of the protein.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

7. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr J F Vollano whose telephone number is (703) 305-4483. The examiner can normally be reached on Monday to Thursday from 6:30 to 5:00 .

9. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter , can be reached on (703)308-4532 . The official fax phone number

for the organization where this application or proceeding is assigned is (703)308-4556. It should be noted that the examiner cannot immediately work on a fax sent to this number.

10. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)308-1235.

Jean F. Vollano

Primary Examiner

Art Unit 1621

June 15, 2003